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WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
DEVI, SARVAMANGALA J N	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,790	PIER ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *0908/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-21,23-25,42 and 86-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-21,23-25,42 and 86-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 09/08/09 in response to the non-final Office Action mailed 03/06/09.

Status of Claim(s)

2) Claims 1, 2, 21, 23-25, 86 and 87 have been amended via the amendment filed 09/08/09.

Claim 22 has been canceled via the amendment filed 09/08/09.

New claim 99 has been added via the amendment filed 09/08/09.

Claims 1, 2, 4-21, 23-25, 42 and 86-99 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claim 22 made in paragraph 15 of the Office Action mailed 03/06/09 under 35 U.S.C § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

6) The rejection of claim 22 made in paragraph 17 of the Office Action mailed 03/06/09 under the judicially created doctrine of obviousness-type double patenting over claim 1 of the US patent 7,252,828 (of record) ('828) under the judicially created doctrine of obviousness-type double patenting over claim 9 of the US patent 7,252,828 (of record) ('828), is moot in light of Applicants' cancellation of the claim.

7) The rejection of claim 22 made in paragraphs 19(c) and 19(d) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 22 made in paragraph 21 of the Office Action mailed 03/06/09 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Pier *et al.* (US patent 7,252,828, of record) ('828), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

9) The rejection of claim 2 and the dependent claims 12, 13 and 19 made in paragraph 15 of the Office Action mailed 03/06/09 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of claims 21, 86 and 97 made in paragraph 16 of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn in light of Applicants' amendment to the claims.

11) The rejection of claim 42 made in paragraph 19(a) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claims 86 and 87 made in paragraph 19(b) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

13) The rejection of claims 23 and 24 made in paragraph 19(e) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

14) The rejection of claims 87-97 and 25 made in paragraph 19(f) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

15) The rejection of claims 1, 2, 4-6, 8-17, 19-21, 23-25, 86-94 and 96-98 made in paragraph 17 of the Office Action mailed 03/06/09 under the judicially created doctrine of obviousness-type double patenting over claim 1 of the US patent 7,252,828 (of record) ('828) and the rejection of claims 18, 42 and 95 made in paragraph 17 of the Office Action mailed 03/06/09 under the judicially created doctrine of obviousness-type double patenting over claim 9 of the US patent 7,252,828 (of record) ('828), is withdrawn.

16) The rejection of claims 1, 2, 4-6, 8-21, 23-25, 42 and 86-98 made in paragraph 21 of the Office Action mailed 03/06/09 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Pier *et al.* (US patent 7,252,828, of record) ('828), is withdrawn. New art rejections are set forth below to address the claims as amended.

Rejection(s) Maintained

17) The rejection of claims 1, 21 and the dependent claims 4-11, 14-18, 20, 23-25, 42 and 98 made in paragraph 15 of the Office Action mailed 03/06/09 under 35 U.S.C § 112, first paragraph, as containing new matter, is maintained for the reasons set forth therein and herein below.

The new dependent claim 99 is now added to this rejection.

Applicants submit the following arguments:

(a) The previously pending claims were directed to polysaccharides which are themselves polymers, which comprised beta 1,6-glucosamine polymers. Such polymers could have been entirely beta 1,6-glucosamine polymers or they could have comprised of such polymers as well as other moieties. In either event, the polymer is still a polysaccharide as it comprises multiple glucosamine monomers. Therefore, Applicants contemplated and had possession of isolated beta 1,6-glucosamine polymers and the previously pending and the original claims provide support for claim 1. (b) The specification at lines 16-21 of page 3 provides an example of a glucosamine polymer. The specification at lines 21-25 of page 4 states that the polysaccharide may be a hetero-substituted polymer, wherein the R groups are a mixture of acetate substitutions (i.e., -NH-CO-CH3) and unsubstituted amine (i.e., -NH2) groups, provided that less than 50% of these groups are substituted with acetate. (c) The specification at lines 15-19 of page 5 teaches that 'The carrier compound may be a polysaccharide and that in some embodiments the carrier polysaccharide is not an N-acetyl beta 1-6 glucosamine'. The specification at lines 10-11 of page

18 contemplated that the carrier compound could be a polysaccharide or a polymer and therefore Applicants amended claim 25 to recite polymers in order to be consistent with such teaching.

Applicants' arguments have been carefully considered, but are not persuasive. Contrary to Applicants' assertion, the previously pending claims 1 and 21 were not directed to polysaccharides, but a composition comprising 'an isolated polysaccharide comprising a beta 1,6-glucosamine polymer'. For example, the original claim 1 was not directed to polysaccharides, but a composition comprising 'an isolated polysaccharide comprising a beta 1,6-glucosamine polymer'. The specification at line 16-21 of page 3 describes the structure of 'the isolated polysaccharide' wherein less than 50% of the R groups are $-NH-CO-CH_3$. The specification at lines 21-25 of page 4 also describes 'the polysaccharide'. With the amendment to claim 1, the claimed composition (inclusive of a vaccine composition) now comprises more than one isolated beta 1,6-glucosamine polymers, wherein less than 40% of glucosamine amino groups are substituted with acetate. This means that the composition encompasses one that comprises pleural isolated beta 1,6-glucosamine polymers with varying degrees of acetate substitution, such that a total of less than 40% of glucosamine amino groups in the pleural polymers are substituted with acetate. However, the parts of the specification pointed to by Applicants do not provide descriptive support for such a composition, or a composition of said scope. The rejection stands.

Claim 25 was amended wherein the carrier polysaccharide compound is now required not to be an N-acetyl beta-l,6-glucosamine 'polymer' as opposed to the previously recited 'N-acetyl beta-l,6-glucosamine'. Contrary to Applicants' assertion, lines 10 and 11 of page 18 state that: 'Carrier compounds include but are not limited to proteins, or peptides, polysaccharides, nucleic acids, or other polymers, lipids, and small molecules', and do not provide support for the negative limitation in the amended claim 25: 'the carrier compound is a polysaccharide that is not an N-acetyl beta-1,6-glucosamine polymer'. Likewise, lines 15-19 of page 5 of the specification and the original claim 25 are supportive of the carrier compound being a polysaccharide that 'is not an N-acetyl beta-1,6-glucosamine', but not N-acetyl beta-1,6-glucosamine polymer. The rejection stands.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Written Description)

18) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19) Claims 20, 42, 97 and 99 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The written description requirement can be met by describing the claimed subject matter to a person skilled in the art using sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002). Sufficient description to show possession of a genus may be achieved by means of recitation of a representative number of polysaccharide or polymers-containing composition species falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may *not* be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Instant claims are not drawn to a screening reagent. The dependent claim 20 is drawn to a composition comprising the isolated pleural polymers of claim 1 wherein the polymers are formulated as 'a vaccine'. The dependent claim 97 is drawn to the isolated polysaccharide of claim 86 which is formulated as 'a vaccine'. Claims 42 and 99 are drawn to a pharmaceutical composition comprising the isolated pleural polymers of claim 1 wherein the polymers are required to 'stimulate an immune response in a subject' against any generic bacteria that make

native PNAG or against any species of *Staphylococci* that make the native PNAG. The recited 'PNAG' is not required to have the same structure as that recited in the base claims. Thus, the instantly claimed 'composition' or 'pharmaceutical composition' does not exclude, but necessarily includes a vaccine. Note that a vaccine 'must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough'. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The isolated beta-1,6-glucosamine polymers or the isolated polysaccharide comprising a beta-1,6-glucosamine polymer, having less than 40% or less than 50% of glucosamine amino groups substituted with acetate, with or without being conjugated to a generic carrier compound, a protein or a peptide carrier compound, is therefore required to trigger an immunoprotective immune response in the host vaccinated therewith. The claimed product thus represents a huge genus of beta 1-6-glucosamine polymers or polysaccharides having 0 to 39.99% or 0 to 49.99% of glucosamine amino groups substituted with acetate. Note that the n in the pleural polymers that are comprised in the composition of claims 20, 42 and 99 can be at least 500. The length of each of the polymers can be at least 500 monomer units and their molecular weight is at least 500,000 Daltons. Note that the term 'at least' has no upper limit. Each of these isolated polymers being conjugated to a carrier compound is within the scope of the claims as indicated via the dependent claim 15. Therefore, the composition of these claims is allowed to contain multiple polysaccharides of unlimited n, unlimited monomers or length, and unlimited molecular weight, wherein 0 to less than 40% of the amino groups are substituted with acetate, wherein each of the polymers is conjugated to a carrier compound, such as a macromolecular tetanus toxoid. However, Applicants never had possession of such a composition which concurrently had the above-identified requisite functions. The solubility, let alone immunogenicity and immunospecific protective capacity against PNAG-making bacteria, of such a composition is simply not predictable. The as-filed specification fails to correlate the structure of such a composition with the requisite functions, i.e., vaccine (prophylactic) functions and stimulation of an immune response in a subject, including a human subject, against staphylococcal or non-staphylococcal bacteria that make native PNAG.

A review of the instant specification indicates that the only composition species that Applicants had in their possession at the time of the invention was a purified staphylococcal

dPNAG species having 15-20% acetate substitutions, wherein the dPNAG was conjugated to diphtheria toxoid or tetanus toxoid protein carrier species. See Example 2. This single species when administered to rabbits along with Freund's adjuvants induced opsonic antibodies to some specific *S. aureus* strains and a specific *S. epidermidis* strain. See Examples 4-6 and Figures 4-6 and 9. However, the description of this single species within the claimed genus may not be sufficient to support the patentability of the vast genus having the requisite function under 35 U.S.C § 112, first paragraph. See *University of California v. Eli Lilly & Co.*, 119 F.3d 15559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). A sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention', which is lacking in the instant case. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). Applicants should note that written description requires more than a mere statement that something is a part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Other than a staphylococcal dPNAG with 15-20% of acetate substitutions, a representative number dPNAG having acetate substitutions encompassed within the recited broad range of zero to less than 40% or 50% has not been correlated with the *requisite* vaccine function and the requisite immunoprotective specificity to any generic bacteria that make native PNAG or against any species of *Staphylococci* that make the native PNAG. Without a concrete structure-function correlation, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ..... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). Applicants were not in possession of a representative number of compositions or vaccines of dPNAG containing varying degrees of acetate substitution spanning the broad range of 0 to less than 40% or 50%, wherein the compositions or vaccines induced protective or opsonic antibodies against homologous or heterologous *Staphylococci* making or not making PNAG and against any other bacteria making PNAG. This is critically important because the effect of 0%, 0-15%, or 20 to less than 40% or less than 50% acetate substitution within the dPNAG on the immunogenicity, opsonogenicity, and/or immunospecific protection in

human or non-human subjects, or in an art-accepted animal model, is not predictable. The precise degree of acetate substitution in dPNAG needed for the protective vaccine functions was neither known nor predictable at the time of the invention. Even as of October, 2005, about three years after the effective filing date of the instant application, the state of the art indicated lack of knowledge or predictability as to whether a PNAG with an intermediate amount of acetylation between native PNAG and dPNAG might have superior and/or highly desirable immunogenic properties. For example, see the teachings of Maira-Litran *et al.* (*Infect. Immun.* 73: 6752-6762, October 2005) at paragraph bridging pages 6760 and 6761. Maira-Litran *et al.* (October, 2005) teach that the role of acetylation in bacterial polysaccharides in the induction of protective antibodies is antigen specific. Maira-Litran *et al.* (October, 2005) further teach that '.... there are examples with different bacterial capsular polysaccharides indicating that the acetate substituents either are of no consequence, interfere with eliciting protective antibody, or are required for generating protective antibody'. See left column of page 6760. Even as of October, 2005, the only staphylococcal dPNAG that was known to induce the most effective specific staphylococcal killing and induce protective antibodies was the one having 15% acetate substitution. See last paragraph under 'Discussion' of Maira-Litran *et al.* (October, 2005). Clearly, instant claims do not meet the provision of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

20) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

21) Claims 21, 23-25, 42 and 86-97 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 42, as amended, and the new claim 99 are vague and indefinite in the use of the abbreviation in the claim: 'PNAG', because it is unclear what it stands for. It is suggested that Applicants recite the abbreviation as a full terminology at first occurrence in the base claim, with its abbreviated recitation retained within parentheses.

(b) Claims 21, 86 and 87 are indefinite and confusing in the limitation: 'beta-1,6-glucosamine polymers .... the isolated polymer ... the .... structure'. Each of the claimed product is recited as containing a carrier compound or a linker joined to a carrier compound, which encompasses a macromolecular carrier compound such as tetanus toxoid. It is unclear how the protein or other carrier compound-containing structure depicted in these claims can be referred to as the structure of beta-1,6-glucosamine polysaccharide or polymer. Is the structure depicted in these claims of a beta-1,6-glucosamine polymer(s) conjugate? Clarification is requested.

(c) Claims 23 and 24, as amended, are indefinite because these claims lack proper antecedent basis in the limitation: 'only one of said'. These claims depend from claim 21, which already includes the limitation 'only one of said'. For proper antecedent basis, it is suggested that Applicants replace the above-identified limitation with the limitation --the only one of said--.

(d) Claims 23-25, which depend from claim 21 and claims 87-97, which depend from claim 86, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

22) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

23) Claims 86, 88, 92-95 and 97 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Joyce *et al*. (US 7,157,443).

It is noted that the limitation 'at least ..... Daltons' has no upper limit and therefore encompasses any number above 800.

Joyce *et al*. taught an isolated *S. aureus* exopolysaccharide having the formula recited in claim 1 therein, wherein 40-60% of R1 is H and the remainder of R1 (i.e., the R in the instantly

recited structure) is $COCH_3$ (i.e., 60-40% and therefore encompasses less than 50% or less than 45%) and 75-95% of R2 in OR2 (i.e., Y1 in the instantly recited structure) is H and the remainder of R2 is an O-linked succinate and n is such that the molecular weight is at least about 300,000 Da. An immunogenic composition (i.e., vaccine) comprising said polysaccharide in a physiologically acceptable salt solution (i.e., physiologically acceptable carrier) is taught. See claims 1 and 5 of Joyce *et al*. Since the broadly recited carrier compound is not limited to a peptide carrier (see Applicants' specification at line 28 of page 4), the succinate present in the prior art polysaccharide qualifies as and is viewed as a carrier compound.

Claims 86, 88, 92-95 and 97 are anticipated by Joyce *et al*.

24) Claims 2, 12, 13, 21, 23-25, 86-95 and 97 are rejected under 35 U.S.C. 102(a) as being anticipated by Yang *et al*. (*Tetrahedron Lett*. 43: 7561-7563, October 2002).

The term 'vaccine' in claim 97 represents the intended use of the claimed product and is not given patentable weight in this rejection.

Yang *et al*. taught an isolated synthetic (1->6)-beta-D-glucosamine hexasaccharide composition having bioactivities for *in vivo* use. The prior art (1->6)-beta-D-glucosamine hexasaccharide lacks acetate substitution and therefore meets the instant limitation: less than 40%, less than 5% etc. of the glucosamine amino groups substituted with acetate. The prior art (1->6)-beta-D-glucosamine is a hexasaccharide and therefore meets the instant limitation: 'n is …. at least four', 'length of … at least 6' and therefore necessarily has a molecular weight recited in the instant claims. The tetrasaccharide or the pentasaccharide(1->6)-beta-D-glucosamine in the prior art compound is joined or linked to the sixth unit, i.e., a carrier compound. See title; abstract; and the entire document including the last product in Scheme 2.

Claims 2, 12, 13, 21, 23-25, 86-95 and 97 are anticipated by Yang *et al*.

Rejection(s) under 35 U.S.C § 103

25) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

26) Claim 19 is rejected under 35 U.S.C § 103(a) as being unpatentable over Joyce *et al.* (US 7,157,443) as applied to claim 2 above.

The teachings of reference of Joyce *et al.* is applied in this rejection because it qualifies as prior art under subsection (e) or (a) of 35 U.S.C. § 102 and accordingly is not disqualified under U.S.C. 103(a).

The teachings of Joyce *et al.* are explained above which do not expressly disclose that their composition is sterile. However, Joyce *et al.* taught that *S. aureus* are human pathogens and that their immunogenic composition, i.e., vaccine, specifically includes human vaccine. See first paragraph under 'Background of the Invention' and second full paragraph in column 3.

Rendering an art-known product sterile was routine and conventional in the art at the time of the invention using a routine art-known sterilization procedure such as sterile filtration or production of the composition under sterile GMP conditions. Given that Joyce's immunogenic composition is meant for *in vivo* use in humans, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to render Joyce's immunogenic composition sterile using any art-known sterilization procedure to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the purpose of providing Joyce's composition in a sterile form suitable for *in vivo* administration to subjects including humans.

Claim 19 is *prima facie* obvious over the prior art of record.

27) Claims 19 and 96 are rejected under 35 U.S.C § 103(a) as being unpatentable over Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002) as applied to claims 2 and 86 above.

The teachings of Yang *et al.* are explained above which do not expressly disclose that their composition is sterile.

However, rendering an art-know product sterile was routine and conventional in the art at the time of the invention using a routine art-known sterilization procedure such as sterile filtration or production under sterile GMP conditions. Given that Yang's composition is meant for *in vivo* use, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to render Yang's composition sterile using an art-known sterilization procedure to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the purpose of providing Yang's composition in a sterile form suitable for *in vivo* administration.

Claims 19 and 96 are *prima facie* obvious over the prior art of record.

Relevant Art

28) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure.

- The concept and the routine process of deacetylating glucosamine polymers were known in the art since the 1950s. For instance, Delangre *et al.* (US 2,842,049) taught deacetylating such polymers. See entire document including column 2.
- At the time of the invention, the structure of the beta-D-amino polyoligoglucosan or glucoside with 1-6 linkage was known and the product was synthesized for use in pharmaceutical compositions. See the English abstract of the Chinese patent application 01136484 of Du Yuguo published 04/17/2002.
- Defaye *et al.* (FR 2,640,628, Applicants' IDS) taught the preparation of beta-(1->6) oligomers of 2-acetamido-2-deoxyglucoses as drugs. See enclosed English abstract.

Remarks

29) Claims 1, 2, 4-21, 23-25, 42 and 86-99 stand rejected.

30) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

31) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

32) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

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